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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,981	02/28/2000	IZUO AOKI	145084	7006
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EXAMINER PUTTLITZ, KARL J				
ART UNIT 1621		PAPER NUMBER		
NOTIFICATION DATE 12/13/2012		DELIVERY MODE ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

09/486,981

Applicant(s)

AOKI ET AL.

Examiner

KARL J. PUTTLITZ

Art Unit

1621

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2012.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 35, 36, 39-43 and 46-49 is/are pending in the application.
- 5a) Of the above claim(s) 42 and 43 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 35, 36, 39-41 and 46-49 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 4) ☐ Other: ____.

DETAILED ACTION

The rejection under section 112, first paragraph is maintained and repeated below:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 36, 39-41, 46-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the recited compounds does not reasonably provide enablement for all hydrates, solvates and polymorphs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

"The standard for determining whether the specification meets the enablement requirement [in accordance with the statute] was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without

undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.").

In the instant case, the rejected claims cover all hydrates, solvates, and polymorphs. Given the scope of the claims, the state of the art, and the amount of guidance in the specification, the disclosure does not contain sufficient information to enable one skilled in the pertinent art for recovery of all hydrates, solvates, polymorphs of the recited compounds.

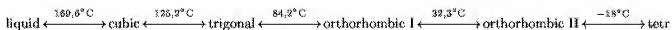
Specifically, the amount of guidance or direction needed to enable an invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. In the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the

accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof."

In the instant case, the state of the art of polymorph or adduct or hydrate recovery is highly unpredictable. See for example *Kirk-Othmer Encyclopedia of Chemical Technology* Copyright © 2002 by John Wiley & Sons, Inc., pp. 95-147, Article Online Posting Date: August 16, 2002. This article indicates that many uncertain factors determine morphology, and specifically that the appearance of the crystalline product and its processing characteristics (such as washing and filtration) are affected by crystal habit (i.e., the general shape of a crystal). Relative growth rates of the faces of a crystal determine its shape. Faster growing faces become smaller than slower growing faces and, in the extreme case, may disappear from the crystal altogether. Growth rates depend on the presence of impurities, rates of cooling, temperature, solvent, mixing, and supersaturation. Furthermore, the importance of each of these factors may vary from one crystal face to another, see page 114.

The reference also teaches that polymorphism or hydration is a condition wherein crystalline form is intimately associated with processing ("*Polymorphism* is a condition in which chemically identical substances may crystallize into different forms. Each form is, however, only stable (thermodynamically) in a certain range of

temperature and pressure. In the case of ambient pressure, eg, ammonium nitrate exhibits four changes in form between -18 and 125 °C:



Transitions from one polymorphic form to another may be accompanied by changes in process conditions (temperature, pressure, shear or solution composition), transitions from one polymorphic form to another and lead to formation of a solid product with unacceptable properties (eg, melting point or dissolution rate).

A specific polymorph may be absolutely essential for a crystalline product, eg., one polymorph may have a more desirable color or greater hardness or disperse in water more easily than another polymorph.”).

Finally the reference teaches that predicting any crystalline form is highly unpredictable, notwithstanding recent advances (“[a] number of studies have shown that various additives can be included in a process stream to alter crystal habit. Prediction of such behavior is difficult and extensive laboratory or bench-scale experiments may be required to evaluate the effectiveness of habit modifiers. More recently, some measure of success has been achieved with altering the habit of organic crystals based on the molecular structure and forces between the crystallizing species or additive with a specific crystal face. Should an additive enhance the properties of a crystalline material, eg, by making it easier to filter, the expense associated with its use may be warranted. Significant efforts toward tailoring additives so that they have specific effects on crystal habit have been made by a number of research groups. The detailed understanding of the chemical interactions at the crystalline interface is necessary to determine the effect

of additives on the crystal growth process. Chemical interactions include van der Waals, ionic, and hydrogen bonding. The influence of "tailor-made additives" on the habit of organic crystals was introduced by Lahav and co-workers and coworkers from the Weizmann Institute, Israel in the 1980s. The reported effect for this group of additives is based on their structural similarity to the crystallizing units. The tailor-made additives are bound at preselected crystal faces and the structurally different sites that are exposed on distinct crystallographic faces. Thus the deposition of incoming crystal layers is hampered. The result is a growth rate reduction of the affected faces and a relative enlargement of its surface areas, since the slowest growing faces always dominate the crystal habit. The development of current computer software for molecular modeling or molecular simulations of crystal structures is based on Donnay and Harker and Hartman and Perdok and Hartman and Bennema approaches. Meanwhile, a number of successful operations is reported based on such computer works. Further developments are needed to save laboratory time and make faster progress in this still difficult and not finally established and understood field of crystallization. [emphasis applied]).

Even other references indicate polymorph recovery is still highly experimental and unpredictable. See, for example, Rouhi, "The Right Stuff, from research and development to the clinic, getting drug crystals right is full of pitfalls", Chemical & Engineering News, February 24, 2003, pp. 32-35. Specifically, the article states that "no method yet exists to predict the polymorphs of a solid compound with significant

certainly. The search for polymorphs is largely an empirical exercise. [emphasis applied]”.

In addition, the state of the art does not support the proposition that any and all solvates of the claimed compound can be prepared since the preparation of solvated solids and crystals is largely empirical, see “Crystallization and Precipitation” in Ullmann’s Encyclopedia of Industrial Chemistry, Copyright © 2002 by Wiley-VCH Verlag GmbH & Co. KGaA, pp. 1-51 (“Laboratory procedures that can be adopted in the preliminary search for possible polymorphs or solvates include: crystallizing from a wide range of solvents (polar, non-polar, hydrophilic, and hydrophobic) at different temperatures; chilling saturated solutions rapidly; precipitation by rapid quenching with a liquid non-solvent; heating excess solid with a high boiling solvent; crystallization from the melt or by sublimation, and so on, see *Id.* at p. 12. However, the instant case goes beyond what is known in the art, because the state of the art for polymorph recovery is very unpredictable, and, as established above, the specification does not offer any guidance on how one of ordinary skill would go about practicing the invention for recovery of every claimed polymorph.

Accordingly, the specification must provide sufficient disclosure regarding isolation of the hydrates, solvates, and polymorphs covered by the rejected claims in order to remedy those deficiencies of the state of the art. However, the specification and the examples do not provide sufficient disclosure that would provide one of ordinary skill guidance to practice isolation of all forms covered by the instant claims. Specifically, the specification only has 9 examples of isolated compounds, much less indicate which

process conditions must be used to select and isolate different forms of hydrates, solvates, adducts and clathrates. M.P.E.P. § 2164.06(b) citing "In *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), [where the court pointed to a] "limited disclosure by appellants of ...particular cyanobacterial genera operative in the claimed invention...." The claims at issue were not limited to any particular genus or species of cyanobacteria and the specification mentioned nine genera and the working examples employed one species of cyanobacteria."

The examiner understands that there is no requirement that the specification disclose every possible embodiment if there is sufficient guidance given by knowledge in the art (See M.P.E.P. § 2164.05(a) "[t]he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).").

However, the instant case goes beyond what is known in the art, because the state of the art for hydrate, solvate, and polymorph recovery is very unpredictable, and, as established above, the specification does not offer any guidance on how one of ordinary skill would go about practicing the invention for recovery of every claimed form.

Accordingly, the requirement for enablement is not met since the claims go far beyond the enabling disclosure, and therefore, based on the forgoing, the rejected claims are prima facie non-enabled.

Applicant argues that none of the claims recite solvates, hydrates or polymorphs. However, the claims are broad enough to include solvates, hydrates or polymorphs, and moreover, clathrates are known to include hydrates, see "Inclusion Compounds" in Kirk-Othmer Encyclopedia of Chemical Technology, Edwin Weber, Published Online: 4 DEC 2000, Copyright © 2001 by John Wiley & Sons, Inc., pp. 1-36 (Inclusion Complexes) at page 7 describing hydrates as clathrates.

Importantly, Inclusion Complexes describes that phenolic clathrates "are capable of including suitably sized guest molecules involving noble gases or other volatile species such as H₂S, SO₂, CO₂, CS₂, HCl, HBr, CH₂Cl₂, and CH₂CHF.", see page 9 of Inclusion Complexes. In this way, the specification has not given any guidance regarding how other compounds, of sizes entirely different than those of the gases described by the reference, can be included in the clathrates covered by the rejected claims.

The rejection under section 112, second paragraph is withdrawn in view of Applicant's amendments.

The rejection under section 102 is maintained since the claims recite mixtures that do not structurally distinguish from the adducts described by the applied references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35 is rejected under 35 U.S.C. 102(b) as being anticipated by DATABASE CAPLUS CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database Accession No. 1960:117924, Abstract of Gladych et al., Journal of the Chemical Society (1960) 2720-6 (Gladych).

Gladych teaches the following adduct:

1,3-Benzenedicarboxylic acid, 4-hydroxy-, compound with 2-aminoethanol (1:1)

Claims 36 is rejected under 35 U.S.C. 102(b) as being anticipated by DATABASE CAPLUS CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database Accession No. 1999:184225, Abstract of Aoki et al., WO 9911609 (WO 609).

WO 609 teaches the following adduct:

Phenol, 4,4'-sulfonylbis[2-(phenylsulfonyl)-, compound with tetrahydrofuran (1:4).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karl J. Puttlitz whose telephone number is (571) 272-0645. The examiner can normally be reached on Monday to Friday from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan, can be reached at telephone number (571) 272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Karl J. Puttlitz/

Primary Examiner, Art Unit 1621